AstraZeneca

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Dockets Management Branch
(HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket Number [2004D-0431]
Response to FDA Call for Comments
Quality Systems Approach to Pharmaceutical cGMP Regulations

Dear Sir or Madam:

Reference is made to the October 4, 2004 Federal Register notice announcing the request for comments on Guidance for Industry: Quality Systems Approach to Pharmaceutical cGMP Regulations.

AstraZeneca congratulates the FDA in maintaining momentum with its Science and Risk based initiatives for Pharmaceutical Development and Manufacturing, including the issue of this guidance, which we view as the first step to modernizing FDA's approach to the manufacture of all medicinal products regulated by the Agency.

The concepts embodied in the draft guidance reflect the Quality System approach undertaken by many pharmaceutical companies, and the document endorses what is in place in those companies. We applaud FDA's efforts in producing this guidance, particularly as it is complemented by the FDA Staff Manual Guide, *Quality Systems Framework for Internal Activities.*

We do have some suggestions for FDA's consideration:

1. The document is written as a companion to the cGMP Regulations found in 21 CFR 210 and 211, appropriately. There are many instances where parts of the cGMPs are referenced, but there is a variable, sometimes incomplete, and therefore potentially misleading, level of information from the CFRs included in this draft guidance. We believe that it would be more effective if the detail currently included were to be removed, and the cGMP expectations or requirements merely referenced. If this is not done, there is a danger that readers will assume that the sections that discuss cGMP requirements are an update of the CFRs, and will then follow the (partial) guidance included herein.

   Examples include: Section IIIF The Quality Unit, which describes some, but not all, of the duties of the Quality Control/Quality Assurance Unit, or Section IV B3 Facilities and Equipment – lines 497-499 – which describe some, but not all, of the (expected) duties of QCU with respect to assuring that facilities and equipment operate effectively.

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2. Many pharmaceutical companies conduct manufacture of APIs and Drug Product on the same site, under the same management and using the same Quality System. Section II C defines the Scope of the guidance but is not clear about its applicability to the manufacture of Active Pharmaceutical Ingredients. It would seem sensible to include API manufacture within the scope of the guidance. This may be implicit in the word 'components' on line 116, but should be made more explicit.

3. In section II B (lines 98-103) and section III E Change Control there is an implication that, by introducing a Quality System as outlined in this guidance, there may be 'shorter and fewer inspections', or that 'manufacturers may be empowered to make changes'. Whilst we welcome such statements, the mechanism for their implementation is unclear, and we request that FDA issue clarification, in the form of guidance, to assist industry in being able to fulfill this expectation.

4. The guidance indicates (lines 94-97) that global harmonization of quality management principles is desirable. AstraZeneca is a strong supporter of this objective and believes that this guidance would make a sound basis for the development of a harmonized quality systems approach to drug manufacture and its control.

5. We suggest that, in the final guidance, references to contemporary activities are removed. Examples include footnotes 4, 5 and 6, which mention current ICH activities that will rapidly become obsolete. We also recommend removing all the adjectives qualifying 'quality system', such as 'robust', 'modern', 'comprehensive'. These tend to confuse and dilute the definition included in the Glossary.

AstraZeneca has contributed to submissions to this Docket by national and international industry associations. Detailed, line-by-line comments have not been repeated here, for clarity's sake, but have been included in those submissions.

Please direct any questions or requests for additional information to me, or in my absence, to Robert Orzolek, Senior Director Regulatory Affairs, at (302) 886-4550.

Sincerely,

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